Emergence and Persistent Dominance of SARS-CoV-2 Omicron BA.2.3.7 Variant, Taiwan

Pei-Lan Shao,[1] Hsiao-Chen Tu,[1] Yu-Nong Gong,[1] Hung-Yu Shu, Ralph Kirby, Li-Yun Hsu, Hui-Yee Yeo, Han-Yueh Kuo, Yi-Chia Huang, Yung-Feng Lin, Hui-Ying Weng, Yueh-Lin Wu, Chien-Chih Chen, Tzen-Wen Chen, Kuo-Ming Lee, Chung-Guei Huang, Shin-Ru Shih, Wei J. Chen, Chen-Chi Wu, Chong-Jen Yu, Shih-Feng Tsai

Since April 2022, waves of SARS-CoV-2 Omicron variant cases have surfaced in Taiwan and spread throughout the island. Using high-throughput sequencing of the SARS-CoV-2 genome, we analyzed 2,405 PCR-positive swab samples from 2,339 persons and identified the Omicron BA.2.3.7 variant as a major lineage within recent community outbreaks in Taiwan.

The COVID-19 pandemic, caused by SARS-CoV-2, originated in China in late 2019, probably in the city of Wuhan (*1*,*2*). The outbreak of this unusual respiratory disease led to a wide variety of responses by various countries across the world (*3*–*6*). The response in Taiwan was rapid and based on both its proximity to China and its experiences during the SARS pandemic ≈2 decades earlier (*5*,*7*,*8*). The introduction of strict travel restrictions on incoming air and sea passengers, long compulsory quarantine periods for the few residents allowed to enter Taiwan, and a vast public acceptance of safety measures (e.g., social distancing, temperature checks, mask wearing) resulted in a delay in the emergence of the COVID-19 pandemic in Taiwan compared with other countries (*5*,*9*,*10*). Until April 2022, there were only limited outbreaks, all of which were quickly contained. Taiwan therefore provides a unique opportunity to explore what happened when the Omicron variant finally evaded the controls put in place by the Taiwan government and began to spread through the country's population.

Residents of Taiwan had not been exposed, on a large scale, to any of the virus variants before Omicron. By the time SARS-CoV-2 began to spread widely in Taiwan April 2022, there had been around 17,000 recorded cases of COVID-19 in the country, and most of them were linked to the Alpha variant (almost all cases in our study had not been infected with SARS-CoV-2 before). Vaccination rates of Taiwan's population at that time were 82.7% having received 1 dose, 78% having received 2 doses, and 59.1% having received 3 doses. The vaccines used in Taiwan before May 2022 were the Oxford-AstraZeneca vaccine (https://www.astrazeneca.com), the Pfizer-BioNTech vaccine (https://www.pfizer.com), the Moderna vaccine (https://www.modernatx.com), the Johnson & Johnson/Janssen vaccine (https://www.jandj.com), and The Median vaccine (a protein subunit COVID-19 vaccine made in Taiwan). Most residents of Taiwan received doses of the first 3 vaccines.

Author affiliations: National Taiwan University Hospital Hsin-Chu Branch, Hsin-Chu, Taiwan (P.-L. Shao, L.-Y. Hsu, H.-Y. Yeo, H.-Y. Kuo, Y.-C. Huang, C.-C. Wu, C.-J. Yu); Institute of Molecular and Genomic Medicine, National Health Research Institutes, Miaoli, Taiwan (H.-C. Tu, Y.-F. Lin, S.-F. Tsai); Research Center for Emerging Viral Infections, Chang Gung University College of Medicine, Taoyuan, Taiwan (Y.-N. Gong, K.-M. Lee, C.-G. Huang, S.-R. Shih); Linkou Chang Gung Memorial Hospital, Taoyuan (Y.-N. Gong, K.-M. Lee, C.-G. Huang S.-R. Shih); Chang Gung University College of Medicine, Taoyuan (Y.-N. Gong, K.-M. Lee, C.-G. Huang, S.-R. Shih); Chang Jung Christian University, Tainan, Taiwan (H.-Y. Shu); National Yang Ming Chiao Tung University, Taipei, Taiwan (R. Kirby, H.-Y. Weng, S.-F. Tsai); National Yang-Ming University, Taipei (H.-Y. Weng); TMU Research Center of Urology and Kidney, Taipei Medical University, Taipei, Taiwan (Y.-L. Wu); Wei-Gong Memorial Hospital, Miaoli, Taiwan (Y.-L. Wu, C.-C. Chen, T.-W. Chen,); Center for Neuropsychiatric Research, National Health Research Institutes, Miaoli (W.-J. Chen); Institute of Epidemiology and Preventive Medicine, National Taiwan University College of Public Health, Taipei (W.-J. Chen); National Taiwan University College of Medicine, Taipei (C.-C. Wu)

DOI: http://doi.org/10.3201/eid2904.221497

[1]These authors contributed equally to this article.

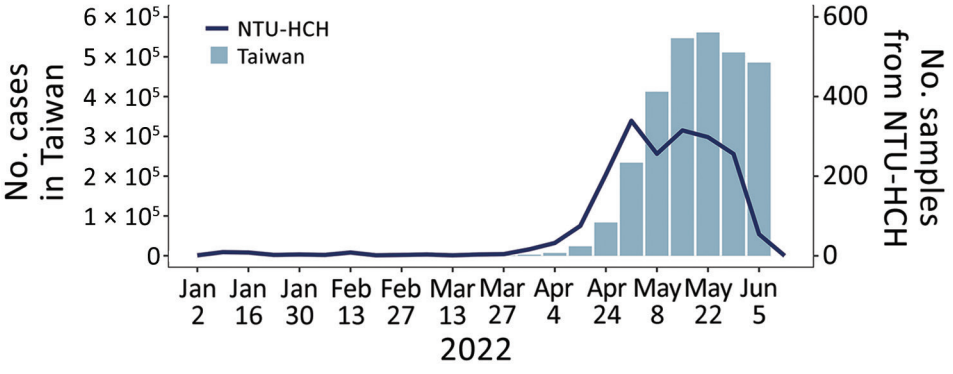


Figure 1. Weekly statistics for confirmed COVID-19 cases in Taiwan and sequenced samples, lineage distribution, and mutation prevalence derived from the NTU-HCH surveillance program, January–June 2022. Graph shows the number of COVID-19 confirmed cases in Taiwan and the sequenced samples from NTU-HCH from January (epidemiologic week 1) to early June (epidemiologic week 23). This figure was constructed using the publicly available data of Taiwan Centers for Disease Control (https://nidss.cdc.gov.tw/nndss/disease?id=19CoV). NTU-HCH, National Taiwan University Hospital–Hsinchu Branch.

Very few COVID-19 cases occurred in Taiwan during 2020 and 2021. Clustered infections were reported in May and June 2021, mainly in northern Taiwan. Even at the peak, only hundreds of positive cases were recorded by Taiwan's Centers for Disease Control. Early in 2022, several Omicron infection clusters were noted, first in northern Taiwan, and new cases quickly followed, soon exceeding 50,000 per day, with outbreaks affecting the entire country (Figure 1) (Infectious Disease Statistics Query System, https://nidss.cdc.gov.tw/nndss/disease?id=19CoV).

The Study

To gain insights into community transmission and to monitor viral evolution, we deployed a genomic surveillance protocol at National Taiwan University Hospital Hsinchu Branch (NTU-HCH) whereby we performed whole-genome sequencing on nasal swab samples detected by PCR to be positive for SARS-CoV-2 (Appendix 1, https://wwwnc.cdc.gov/EID/article/29/4/22-1497-App1.pdf). To ensure data quality, we submitted genomic data to GISAID (https://www.gisaid.org) only on those sequences that had >98% coverage of the 29,903-bp SARS-CoV-2 target genome. We used the same set of high-quality sequences for tracking the signature mutations in the viral samples (Table 1) and for phylogenetic analysis (Figure 2; Appendix 1, Figure 1). We found 2,405 samples among 5 batches that met the above criterion and this generated 2,043 sequences (84.9% pass rate). We selected 1,966 sequences for GISAID submission (Appendix 1 Table 1).

We analyzed the assembled viral genome sequences (Appendix 1 Table 2) and tracked the lineages and nonsynonymous amino acid changes in the Omicron samples collected during 2022 (Appendix 1 Figures 2, 3). Comparing the later 3 datasets (batches 3–5), we discovered that 3 amino acid changes (open reading frame [ORF]1a: L631F; spike (S): K97E; nucleocapsid; M322I) occurred only after the fourth sequencing batch. The percentage of sequences containing the signatures progressed steadily from 62% in batch 4 to 85% in batch 5. All batch-3 isolates belonged to the BA.1 or BA.2 classification, suggesting that the rapid increase of cases in Taiwan in April and May 2022—from 0 cases/day to ≈100,000 cases/day—came from a strain (BA.2.3.7) that might have been involved in a founder effect.

To construct the framework of the phylogenetic tree, we took 1,966 genome sequences from our study and analyzed them in the global context of 881 GISAID reference sequences (Figure 2; Appendix 2, https://wwwnc.cdc.gov/EID/article/29/4/22-1497-App2.xlsx). We then zoomed in and compared the 1,577 Omicron sequences of our study against the 228 Omicron BA.2.3.7 strains from GISAID. Those sequences were reported from 21 countries, including 51 from Taiwan (Table 2). We conducted phylogenetic analysis using the Pango-dynamic nomenclature system (*11*).

We found evidence that this novel lineage BA.2.3.7 with 3 amino acid changes (ORF1a: L631F; S: K97E; and nucleocapsid: M322I) was circulating dominantly in Taiwan over the study period. Of note, the first BA.2.3.7 strain identified in the epidemic in Taiwan was collected on March 27, 2022, and since that time we detected several genomic changes affecting this Omicron lineage. For example, we noted a new mutation, G1251V (Appendix 1 Figure 3, green line) in the S protein, from April onward, and that particular circulating lineage then rapidly spread across Taiwan.

Conclusions

We acknowledge that our study is limited in that we conducted the genomic surveillance in only 1 medical center; therefore, the observed dominance of BA.2.3.7 might be due to clustering of cases. Of note, while this

Table 1. Signature mutations in SARS-CoV-2 BA.2.3.7 sublineages of viral samples from a study of the Omicron BA.2.3.7 variant in community outbreaks, Taiwan

	Accumulated mutations*			
Lineage	BA.2	BA.2.3	BA.2.3.7	Selected mutations†
ORF1a	S135R	S135R	S135R	NA
	NA	NA	NA	A591V
	NA	NA	L631F	L631F
	T842I	T842I	T842I	NA
	NA	NA	NA	I1091T
	G1307S	G1307S	G1307S	NA
	NA	A2909V	A2909V	NA
	L3027F	L3027F	L3027F	NA
	T3090I	T3090I	T3090I	NA
	L3201F	L3201F	L3201F	NA
	NA	NA	NA	T3224A
	T3255I	T3255I	T3255I	NA
	P3395H	P3395H	P3395H	NA
	del3675	del3675	del3675	NA
	del3676	del3676	del3676	NA
	del3677	del3677	del3677	NA
	NA	NA	NA	V3683I
Spike	T19I	T19I	T19I	NA
	L24S	L24S	L24S	NA
	del25	del25	del25	NA
	del26	del26	del26	NA
	del27	del27	del27	NA
	NA	NA	K97E	K97E
	G142D	G142D	G142D	NA
	V213G	V213G	V213G	NA
	G339D	G339D	G339D	NA
	S371F	S371F	S371F	NA
	S373P	S373P	S373P	NA
	S375F	S375F	S375F	NA
	T376A	T376A	T376A	NA
	D405N	D405N	D405N	NA
	R408S	R408S	R408S	NA
	K417N	K417N	K417N	NA
	N440K	N440K	N440K	NA
	S477N	S477N	S477N	NA
	T478K	T478K	T478K	NA
	E484A	E484A	E484A	NA
	Q493R	Q493R	Q493R	NA
	Q498R	Q498R	Q498R	NA
	N501Y	N501Y	N501Y	NA
	Y505H	Y505H	Y505H	NA
	D614G	D614G	D614G	NA
	H655Y	H655Y	H655Y	NA
	N679K	N679K	N679K	NA
	P681H	P681H	P681H	NA
	N764K	N764K	N764K	NA
	D796Y	D796Y	D796Y	NA
	Q954H	Q954H	Q954H	NA
	N969K	N969K	N969K	NA
	NA	NA	NA	G1251V
ORF3a	NA	L140F	L140F	NA
	T223I	T223I	T223I	NA
Nucleocapsid	P13L	P13L	P13L	NA
	del31	del31	del31	NA
	del32	del32	del32	NA
	del33	del33	del33	NA
	R203K	R203K	R203K	NA
	G204R	G204R	G204R	NA
	NA	NA	M322I	M322I
	S413R	S413R	S413R	NA

*Using SARS-CoV-2 Wuhan-Hu-1 (GenBank accession no. MN908947.3) as the reference sequence. Mutations in ORF1b, E, M, ORF6, and ORF8 are not shown as they are identical between BA.2, BA.2.3 and BA.2.3.7. NA, not applicable; ORF, open reading frame.
†Mutations detected in the Omicron lineages are characterized in this study.

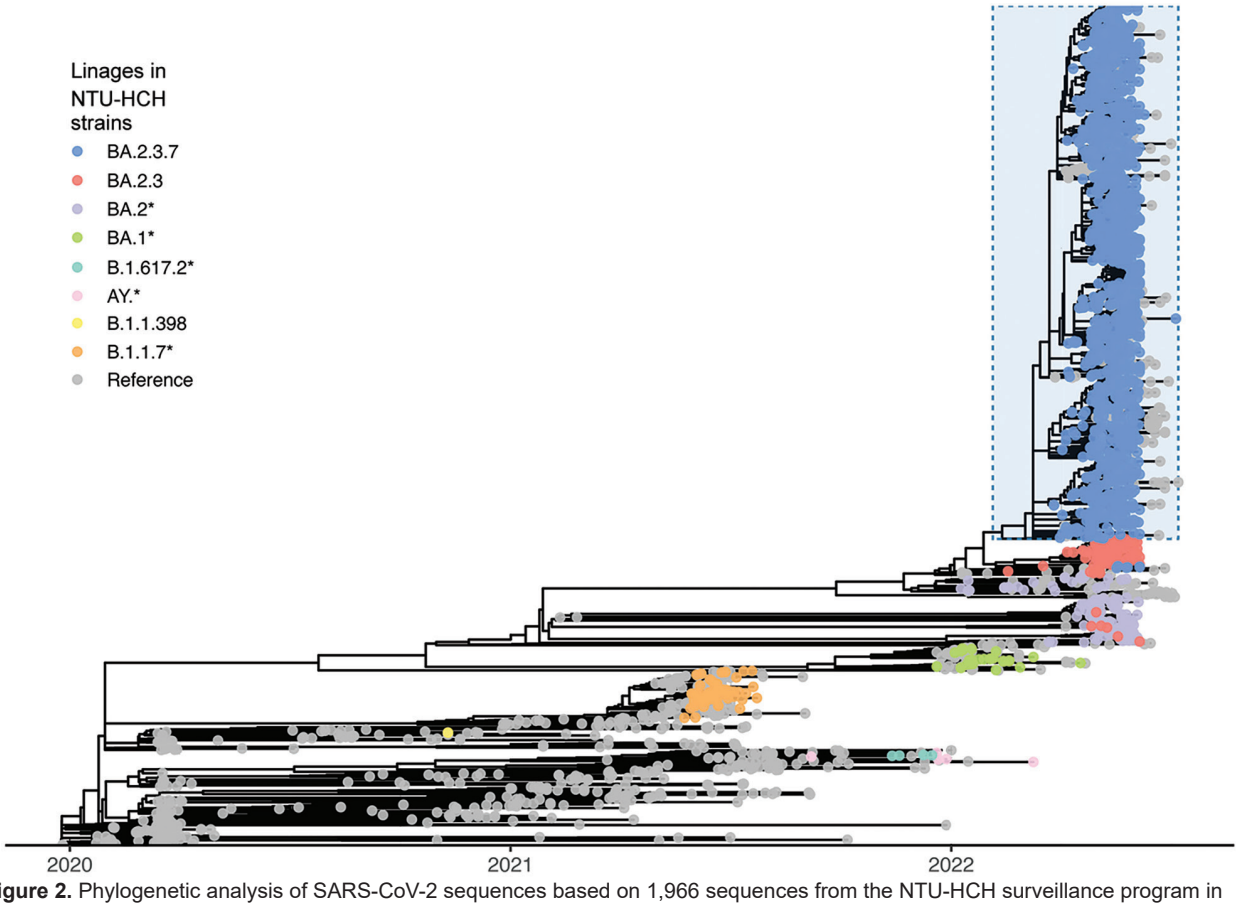


Figure 2. Phylogenetic analysis of SARS-CoV-2 sequences based on 1,966 sequences from the NTU-HCH surveillance program in Taiwan and 881 sequences from GISAID (https://www.gisaid.org). Lineages of NTU-HCH strains are annotated in different colors; asterisks (*) represent the collection of a specific lineage with its sublineage. The BA.2.3.7 strains were dominantly circulating in Taiwan from March 2022, highlighted by light blue in the tree. NTU-HCH, National Taiwan University Hospital–Hsinchu Branch.

paper was in preparation, we became aware that several viral sequences with the same signature mutations had been reported in Taiwan. Although the number of cases was relatively small (51) compared with the number of cases we studied, the 4 locations in Taiwan reporting those cases were different from our collection point at the hospital. Thus, this new lineage appeared to be broadly detectable across Taiwan.

Other Asia-Pacific countries have also recently reported a substantial cumulative prevalence of the BA.2.3.7 variant (Table 2). Among the 44 Omicron BA.2.3.7 strains reported from Japan, 2 of the affected persons had travel history to Vietnam and 41 to Taiwan, suggesting considerable silent outward transmission from Taiwan. In contrast, BA.2.3.7 accounts for <0.5% of the sequences reported in either California, USA, or globally. The emergence of Omicron BA.2.3.7 in Asia is remarkable. Because there are no reliable genomic data from early cases in Malaysia and Vietnam, our phylogenic analysis and the metadata from GISAID suggests that travel between

Table 2. Submitted sequences of SARS-CoV-2 BA2.3.7 from different countries for inclusion in a study of the Omicron BA.2.3.7 variant in community outbreaks, Taiwan

Country	No. sequences
Taiwan	51*
Japan	44
United States	37
Indonesia	27
Hong Kong	22
Australia	7
Denmark	6
Canada	5
Singapore	4
South Korea	4
Philippines	3
Thailand	3
France	3
Cambodia	2
Austria	2
Sweden	2
Germany	2
Spain	1
Vietnam	1
Slovenia	1
New Zealand	1
Total	228

*Number does not include the contributions from this study.

countries in Asia contributed to the rapid spread of this unique Omicron lineage.

In summary, our genomic dataset is uniquely valuable for understanding how a major COVID-19 outbreak occurs in a naive and vaccinated population in Taiwan, a country with a very limited number of entry events. We theorize that the dominant circulation of BA.2.3.7 in Taiwan is likely the result of genetic drift or a founder effect, although it is also possible that increased transmissibility or vaccine evasion played some part. As countries in Asia move from zero tolerance to more open COVID-19 policies, continued surveillance of SARS-CoV-2 using next-generation sequencing is important. Early detection of viral evolution events in endemic areas will help minimize future disruptions caused by a new variant.

Acknowledgments

We extend our thanks to Y. Henry Sun and Hsiao-Hui Tso for critical reading of the manuscript; Yi-Chun Tsai, Shuo-Peng Chou, Jhen-Rong Huang, and Yuan-Yu You for sample collection and nucleic acid preparation; and Tai-Yun Lin, Yu-Chen Huang, and Chiao-Chan Wang for library construction and sequencing operation. We gratefully acknowledge the authors from the originating laboratories responsible for obtaining the specimens as well as the submitting laboratories where the genome data were generated and shared via GISAID and GenBank (Appendix 2).

This work was supported by Ministry of Health and Welfare of Taiwan (MOHW110-TDU-C-222-000010) to S.F.T., by the Research Center for Emerging Viral Infections from The Featured Areas Research Center Program within the framework of the Higher Education Sprout Project by the Ministry of Education of Taiwan, the Ministry of Science and Technology of Taiwan (MOST 111-2321-B-182-001, MOST 111-2634-F-182-001, MOST 110-2222-E-182-004, and MOST 111-2221-E-182-053-MY3), and the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number 5U01AI151698-02 to Y.N.G. and S.R.S.

About the Author

Dr. Shao is an assistant professor in the Department of Laboratory Medicine and Pediatrics, National Taiwan University College of Medicine, Taiwan. Her main research interests include infectious disease, clinical virology, clinical microbiology, and vaccines. Dr. Tu is postdoctoral fellow in the Institute of Molecular and Genomic Medicine, National Health Research Institutes, Taiwan. Her research interests include next generation sequencing technology, cancer, and genomic research. Dr. Gong is an assistant professor in Research Center for Emerging Viral Infections and International Master's Degree Program for Molecular Medicine in Emerging Viral Infections, Chang Gung University, Taiwan. His research interests include bioinformatics, phylogenetics, machine learning, and viral evolution.

References

1. World Health Organization. WHO statement regarding cluster of pneumonia cases in Wuhan, China. January 9, 2020 [cited 2023 Jan 26]. https://www.who.int/china/news/detail/09-01-2020-who-statement-regarding-cluster-of-pneumonia-cases-in-wuhan-china
2. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al.; China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382:727–33. https://doi.org/10.1056/NEJMoa2001017
3. Mathieu E, Ritchie H, Rodés-Guirao L, Appel C, Giattino C, Hasell J, et al. Coronavirus pandemic (COVID-19). Our world in data [cited 2023 Jan 26]. https://ourworldindata.org/coronavirus
4. Jung AS, Haldane V, Neill R, Wu S, Jamieson M, Verma M, et al. National responses to covid-19: drivers, complexities, and uncertainties in the first year of the pandemic. BMJ. 2021;375:e068954. https://doi.org/10.1136/bmj-2021-068954
5. Summers J, Cheng HY, Lin HH, Barnard LT, Kvalsvig A, Wilson N, et al. Potential lessons from the Taiwan and New Zealand health responses to the COVID-19 pandemic. Lancet Reg Health West Pac. 2020;4:100044. https://doi.org/10.1016/j.lanwpc.2020.100044
6. Tsou HH, Kuo SC, Lin YH, Hsiung CA, Chiou HY, Chen WJ, et al. A comprehensive evaluation of COVID-19 policies and outcomes in 50 countries and territories. Sci Rep. 2022;12:8802. https://doi.org/10.1038/s41598-022-12853-7
7. Chen SC. Taiwan's experience in fighting COVID-19. Nat Immunol. 2021;22:393–4. https://doi.org/10.1038/s41590-021-00908-2
8. Wang CJ, Ng CY, Brook RH. Response to COVID-19 in Taiwan: Big data analytics, new technology, and proactive testing. JAMA. 2020;323:1341–2. https://doi.org/10.1001/jama.2020.3151
9. Gong YN, Tsao KC, Hsiao MJ, Huang CG, Huang PN, Huang PW, et al. SARS-CoV-2 genomic surveillance in Taiwan revealed novel ORF8-deletion mutant and clade possibly associated with infections in Middle East. Emerg Microbes Infect. 2020;9:1457–66. https://doi.org/10.1080/22221751.2020.1782271
10. Lin C, Braund WE, Auerbach J, Chou JH, Teng JH, Tu P, et al. Policy decisions and use of information technology to fight coronavirus disease, Taiwan. Emerg Infect Dis. 2020;26:1506–12. https://doi.org/10.3201/eid2607.200574
11. Rambaut A, Holmes EC, O'Toole Á, Hill V, McCrone JT, Ruis C, et al. A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. Nature Microbiology. 2020;5:1403-07. https:// doi.org/10.1038/s41564-020-0770-5

Address for correspondence: Chong-Jen Yu, NTUH, Hsin-Chu Branch, Sec. 1 Shengyi Rd, Zhubei, Hsinchu 30261, Taiwan; email: jefferycjyu@ntu.edu.tw; Shih-Feng Tsai, NHRI, 35 Keyan Rd, Zhunan, Miaoli 35053, Taiwan; email: petsai@nhri.edu.tw

Article DOI: http://doi.org/10.3201/eid2904.221497

Emergence and Persistent Dominance of Omicron BA.2.3.7 Variant, Taiwan

Appendix 1

Additional Material and Methods

METHODS

We applied Illumina COVIDSeq amplicon sequencing technology to the whole-genome analysis of SARS-CoV-2. RNA was extracted from virus-inactivated swab samples. Complementary DNA synthesis was carried out using the reagents provided by the manufacturer, by which the SARS-CoV-2 genome underwent reverse transcription and was then amplified in 98 overlapping amplicons, together with appropriate human controls. In the final optimized procedure, we processed 384 samples at a time, and analyzed the pooled libraries on a single lane of a S4 chip using a NovaSeq6000.

Patients and RNA extraction

Representative samples were collected from National Taiwan University Hospital Hsinchu Branch (NTU-HCH). Before the major outbreak, nearly 300 samples were surveyed in January-April, 2022. On the other hand, we sequenced close to 2000 samples during the major outbreak in May, representing approximately 0.1% of the estimated 2 million confirmed cases of Taiwan. Samples for RNA extraction were collected in 3 mL sterile viral transport medium (VTM) tubes and consisted of 2405 nasopharyngeal swabs belonging to 2339 patients. RNA was prepared by automated extraction using TANBead Nucleic Acid Extraction kits REF M665A46 (Taiwan Advanced Nanotech Inc.) and the QIAsymphony SP protocol (QIAGEN). This study was reviewed and approved by the Research Ethics Committee (110-110-E) of NTU-HCH.

COVIDseq

We carried out the sequencing using Illumina COVIDSeq Test kits (RUO version) according to the manufacturer's instructions. The workflow consists the following steps: cDNA synthesis, then virus target amplification using V3 nCov-2019 primers, followed by library preparation and library pooling. Subsequently, 98 SARS-CoV-2 targets and 11 human targets, the latter acting as controls, were analyzed on a NovaSeq 6000 instrument using 2x151-bp paired-end reads. Next, we used Illumina DRAGEN COVID Lineage app version 3.5.9 (base on pangolin 4.1.2 pangolin-data 1.12 and NextClade 1.11.0) in the BaseSpace Sequence Hub for rapid analysis.

Phylogenetic analysis

A set of 1966 NTU-HCH sequences were deposited to the Global Initiative on Sharing All Influenza Data (GISAID) (*1*) with the following epi accession numbers: EPI_ISL_14192849 to EPI_ISL_14192840, EPI_ISL_14191496 to EPI_ISL_14191488, EPI_ISL_14191320 to EPI_ISL_14190364, and EPI_ISL_14190353 to EPI_ISL_14189364. To investigate the global transmission, 228 BA.2.3.7, 277 global, and 376 additional sequences from Taiwanese were retrieved from GISAID as of July 2022. A total of 2847 sequences, including 1966 from NTU-HCH and 881 reference sequences (Appendix 2: GISAID Acknowledgment) that had met the quality standard, were used for the analysis. The phylogenetic tree was initially constructed using Nextstrain CLI (command-line interface) (version 3.2.5) (*2*) and annotated and visualized using ggtree package (*3*).

References

1. Shu Y, McCauley J. GISAID: Global initiative on sharing all influenza data - from vision to reality. Euro Surveill. 2017;22:30494. PubMed https://doi.org/10.2807/1560-7917.ES.2017.22.13.30494

2. Hadfield J, Megill C, Bell SM, Huddleston J, Potter B, Callender C, et al. Nextstrain: real-time tracking of pathogen evolution. Bioinformatics. 2018;34:4121–3. PubMed https://doi.org/10.1093/bioinformatics/bty407

3. Yu G, Smith DK, Zhu H, Guan Y, Lam TT-Y. ggtree: an r package for visualization and annotation of phylogenetic trees with their covariates and other associated data. Methods Ecol Evol. 2017;8:28–36. https://doi.org/10.1111/2041-210X.12628

Appendix 1 Table 1. Sequences selected for GISAID submission and phylogenetics analysis

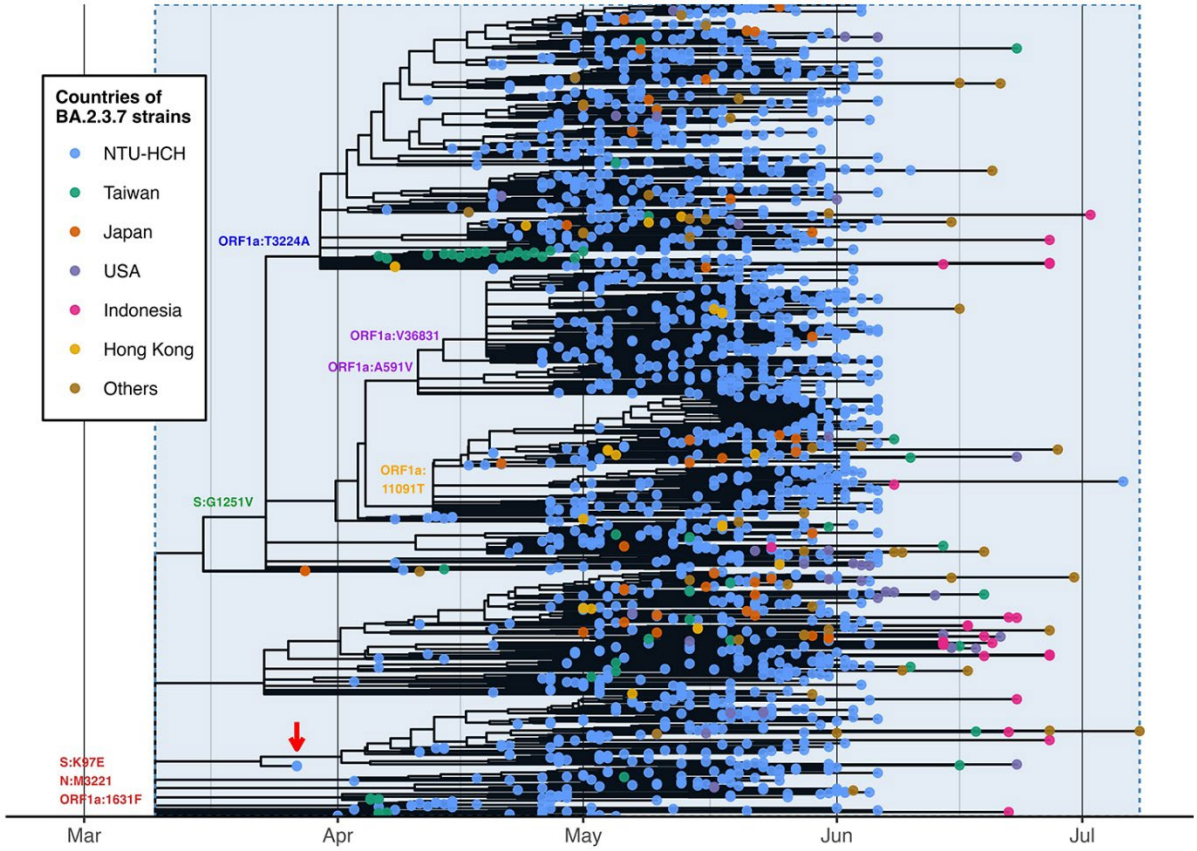
		Coverage						
Batch	**Run**	**≥98**	**90-97**	**80-89**	**70-79**	**60-69**	**<60**	**Total**
1	1	77	12	0	4	0	1	94
2	2	63	0	5	3	4	18	93
3	3	43	14	4	2	5	38	106
4	4	140	17	2	3	0	30	192
5	5A	360	15	5	2	0	2	384
	5B	331	30	11	6	1	5	384
	5C	304	47	15	14	4	0	384
	5D	366	16	2	0	0	0	384
	5E	359	24	0	1	0	0	384
	NTU-HCH*	1966	163	44	31	14	93	2311
	Total†	2043	175	44	35	14	94	2405

*Count of NTU-HCH cases, from Batch (Run-2) through Batch 5 (Runs 5A-5E)
†Total count of all three hospitals

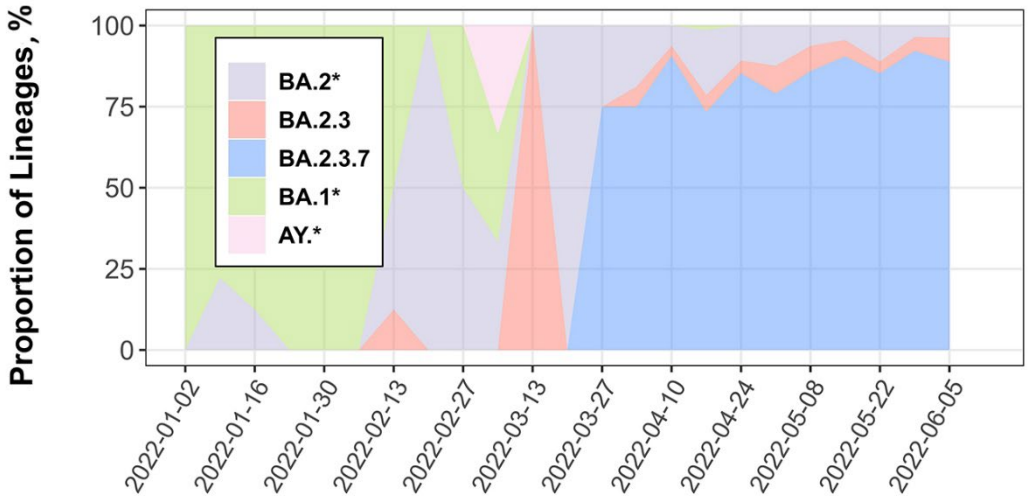
Appendix 1 Table 2. Samples and cases collected for this study as analyzed by the Illumina COVIDSeq system on NovaSeq6000

Batch	Sampling time period	Hospital source	Sample number	Case number	Sequencing run
1st	2021 (May)	WKH 12 CGMH 82	94	93	SP 2x51bp
2nd	2021 (May-July)	WKH 12* CGMH 82* NTU-HCH 93	93†	69†	S4 lane 2x151bp
3rd	2021 (Dec)~2022 (Feb) + 2020 (Nov)~2021 (April~Nov) 11 cases	NTU-HCH 106	106	66	S4 lane 2x151bp
4th	2022 (Feb 25~April 27) + April 27 (1 case)	NTU-HCH 192	192	191	S4 lane 2x151bp (288 sample/ lane)
5th	5A_2022 (April 26~May 3)	NTU-HCH 384	384	384	S4 lane 2x151bp
	5B_2022 (May 3~May 23)	NTU-HCH 384	384	384	S4 lane 2x151bp
	5C_2022 (May 17~June 6)	NTU-HCH 384	384	384	S4 lane 2x151bp
	5D_2022 (May 4~June 6)	NTU-HCH 384	384	384	S4 lane 2x151bp
	5E_2022 (May 18~June 6) + July 6 (1 case)	NTU-HCH 384	384	384	S4 lane 2x151bp

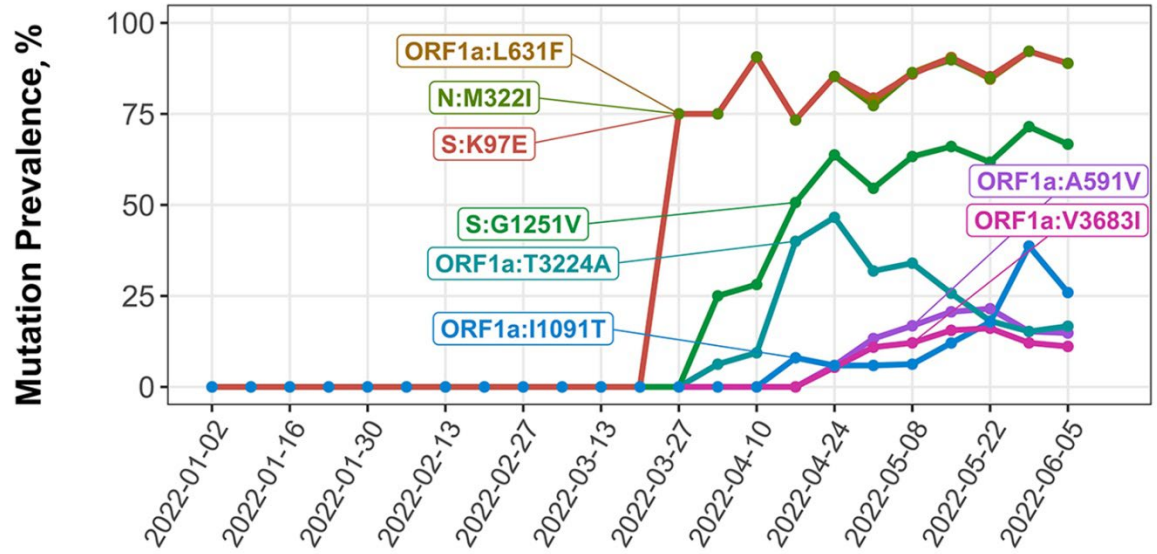
*Repeat from the first batch
†New samples from NTU-HCH



Appendix 1 Figure 1. Analysis of 1577 BA.2.3.7 sequences submitted to GISAID from the current study and 228 BA.2.3.7 sequences deposited to GISAID by other groups. The position of signature mutations are indicated: 3 (S:K97E, N:M322I, ORF 1a:L631F) are located at the origin of the B.A.2.3.7 lineages. S:G1251V is mapped at a major branch in the upper trunk of the tree, under which 3 minor branches can be defined by mutations in ORF1a:T3224A (in blue), ORF1a:A591V and ORF1a:V3683I (in purple), and ORF1a:I1091T (in orange). Sample origins are color coded. Red arrow denotes the index case collected from Taiwan on March 27, 2022.



Appendix 1 Figure 2. Lineage distribution of National Taiwan University Hospital–Hsinchu Branch (NTU-HCH) strains. Most were identified as BA.1 or BA.2 lineages and sublineages annotated with an asterisk (*) before end of March. Since then, the BA.2.3.7 lineage became the dominant variant circulating in Taiwan.



Appendix 1 Figure 3. Proportion of the different signature mutations in January 1–June 6, 2022 derived from a study of the Omicron BA.2.3.7 variant in Taiwan. Note the sharp increase of the Omicron variant 2.3.7 from week 13 (March 27– April 2) onward; the proportion of this Omicron variant remained high for at least 10 weeks. Also note overlapping of the 3 signature mutations (S:K97E, N:M322I, ORF1a:L631F) of BA.2.3.7 and a steady increase of sequences positive for S:G1251V from week 14 (April 3–9), reaching a plateau at week 17 (April 24–30).